REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

Claims 1-19 were pending in this application when last examined.

Claims 1-9 were examined on the merits and stand rejected.

Claims 10-19 were withdrawn as non-elected subject matter.

Claims 2-3, 6-7 and 10-19 are cancelled without prejudice or disclaimer thereto. Applicants reserve the right to file a Continuation or Divisional Application on any cancelled subject matter.

Claim 1 is amended. Support for the amendments to claim 1 can be found as follows:

(1) the scope of "ring A" has been restricted to "an azetidine ring" (basis: compounds (I-1) to (I-7), and (I-1-1) to (I-1-3) described on pages 22-25, and working examples);

(2) the scope of "X" has been restricted to "oxygen" (basis: compounds ((I-1) to (I-7), and (I-1-1) to (I-1-3) described on pages 22-25, and working examples);

(3) the definition of "R^1, R^2, R^3 and R^4" has been restricted to "R^1 and R^2 are each independently C_{1-8} alkyl which may have substituent(s) or a benzene ring which may have substituent(s) (basis: page 21, line 10 from the bottom to line 8 from the bottom, and on the same page, line 5 from the bottom to line 3 from the bottom), R^3 is hydrocarbon group which may have substituent(s) (page 22, lines 6-7), R^4 is hydrogen (basis: page 22, line 15), R^1 and R^2 may be taken together with the adjacent nitrogen atom to form a piperidine, pyrrolidine, morpholine, piperazine, indoline, tetrahydroquinoline or tetrahydroisoquinoline ring group which may have further substituent(s)" (basis: page 22, lines 3-4);

(4) the terms "an N-oxide thereof, a solvate thereof, or a prodrug thereof" have been deleted"; and

(5) finally, the phrase "with the adjacent nitrogen atom" has been amended to conform with the present claims 4 and 5.

Claim 4 is amended. Support for the amendments to claim 5 can be found on page 22, lines 3-4, of the specification as filed.

Claim 9 is amended to clarify the claimed invention.

No new matter has been added.

II. FOREIGN PRIORITY

The Examiner is respectfully requested to fully acknowledge the claim for foreign priority by checking the appropriate boxes in item 12 on page 1 of the next Office Action.

III. INDEFINITENESS REJECTION

On pages 2 and 3 of the Office Action, claim 1 and its dependent claims were rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Applicants respectfully traverse this rejection as applied to the amended claims.

In particular, Applicants note that, without acquiescence to the correctness of the Examiner's rejection, "sulfur and nitrogen" are deleted from the scope of "X". Further, the phrases "a heterocyclic ring group" and "which may have further substituent(s)" in claims 1 and 5 have been further limited to reduce the number of substituents. Finally, the term "prodrug" has been deleted.

Thus, Applicants suggest that this rejection is overcome as applied to the amended claims and should be withdrawn.

IV. ENABLEMENT REJECTION

On pages 3-5 of the Office Action, claims 1 and the dependent claims were rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for making a few of the compounds of formula (I), does not reasonably provide enablement for millions of the possibilities suggested by formula (I). Applicants respectfully traverse this rejection as applied to the amended claims.

In particular, Applicants note that the amended claims are no longer drawn to N-oxides, solvates or prodrugs of the compound of formula (I). Also, X has been limited to oxygen.

Further, in the amended claims, the compounds of formula (I) has been drastically restricted. Thus, Applicants contend that the specification enables any person skilled in the art to which it pertains to make and use the invention commensurate in scope with the amended claims.

In particular, how to make the compounds of formula (I) or salts thereof are fully described on page 32, line 3 from the bottom to page 48, line 15 in the specification. Further, a number of compounds are described at working Examples 1, 2, 3, 3(1)-3(809), 4, 5 and 5(1)-5(122) on pages 47-181.

How to use the compounds of formula (I) or salts thereof are fully described on page 48, line 7 from the bottom to page 66, line 2 from the bottom, and Formulation Examples 1 and 2 on page 222 of the specification.

The compounds of formula (I) are characterized by a 1-aminocarbonyl-4-aminoazetidine skeleton. The present inventors contend that this skeleton contributes to the excellent antagonistic activity against EDG-5.

Antagonistic activity against EDG-5 is shown in Example 3(18), *i.e.* N-[3,5-bis(trifluoromethyl)phenyl]-3-[ethyl(phenyl)amino]-azetidine-1-carboxamide (IC_{50} value = 950 nM), described on page 222, lines 5-6, of the present specification. The compound of Example 3(18) is a representative compound of formula (I) of the claimed invention.

Accordingly, Applicants contend that it is clear that all of the compounds of formula (I) containing a skeleton of 1-aminocarbonyl-4-aminoazetidine show excellent antagonistic activity against EDG-5.

Thus, Applicants respectfully suggest that this rejection, as applied to the amended claims, is untenable and should be withdrawn.

V. ANTICIPATION REJECTIONS

On page 5 of the Office Action, claims 1-7 and 9 were rejected under 35 U.S.C. § 102(b) as anticipated by Bisacchi et al. Applicants respectfully traverse this rejection.

Applicants note that claim 1, as amended, is drawn to a compound of formula (I) wherein ring A is an azetidine ring, X is oxygen, R^1 and R^2 are each independently C_{1-8} alkyl which may have substituent(s) or a benzene ring which may have substituent(s), R^3 is hydrocarbon group which may have substituent(s), R^4 is hydrogen, R^1 and R^2 may be taken together with the adjacent nitrogen atom to form a piperidine, pyrrolidine, morpholine, piperazine, indoline,

tetrahydroquinoline or tetrahydroisoquinoline ring group which may have further substituent(s), or a salt thereof.

Applicants note that the compounds within the scope of formula (I) do not include the compound of Bisacchi et al. shown on page 5 of the Office Action. For instance, it is noted that R^3 and R^4 of Bisacchi et al. fail to meet the limitations of the claimed compound. Thus, this rejection, as applied to the amended claims, is overcome.

Further, on page 6 of the Office Action, claims 1-7 and 9 were rejected under 35 U.S.C. § 102(e) as anticipated by Nakade et al. Applicants respectfully traverse this rejection as applied to the amended claims.

Nakade et al. has an international filing date of June 25, 2003. However, as noted in MPEP 706.02(f)(1)(C)(1), the WO publication must be in English for this to be a 102(e) reference. WO 2004/002531 was not published in English and therefore is not available under 102(e).

Furthermore, Applicants note that this reference was published on August 1, 2004. Enclosed herewith is a certified translation of JP 2003/429948, to which priority has been claimed. Thus, priority has been perfected in the current application to December 25, 2003. This date is before the date of the publication of the WO 2004/002531 publication. Thus, for the above-noted reasons, this rejection is untenable as this reference is unavailable as prior art.

Finally, also on page 6, claims 1-7 and 9 were rejected under 35 U.S.C. § 102(e) as anticipated by Ohki et al. Applicants respectfully traverse this rejection as applied to the amended claims.

Claim 1 as amended, is directed towards a compound of formula (I) wherein ring A is an azetidine ring, X is oxygen, R^1 and R^2 are each independently C_{1-8} alkyl which may have substituent(s) or a benzene ring which may have substituent(s), R^3 is hydrocarbon group which may have substituent(s), R^4 is hydrogen, R^1 and R^2 may be taken together with the adjacent nitrogen atom to form a piperidine, pyrrolidine, morpholine, piperazine, indoline, tetrahydroquinoline or tetrahydroisoquinoline ring group which may have further substituent(s), or a salt thereof.

Applicants note the scope of amended claim 1 does not include the compound of Ohki et al. shown on page 6 of the application. For example, R^3 and R^4 of the compound of Ohki et al.

do not meet the claim limitations. Thus, for the noted reasons, this rejection is untenable and should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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October 8, 2008

ATTACHMENTS

A. Verified English Translation of JP 2003-429948.

VERIFICATION OF TRANSLATION

I, Masayuki Murota, of c/o Ono Pharmaceutical Co., Ltd., 1-1, Sakurai 3-chome, Shimamoto-cho, Mishima-gun, Osaka, JAPAN, state the following:

I am fluent in both the English and Japanese languages and capable of translating documents from one into the other of these languages.

The attached document is a true and accurate English translation to the best of my knowledge and belief of the description and claims of Japanese patent application No.2003-429948.

I state that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true.

Signature: Masayuki Murota

Date: October 3, 2008